REMARKS

Amendments to the Claims

Non-elected claims 1-11 and 20-35 are cancelled without prejudice or disclaimer, and new claims 37-39 are presented herein. Upon entry of this amendment, claims 12-19 and 36-39 will be pending.

Solely in order to expedite prosecution, Applicant has amended the claims to delete the term "amine" from claim 12. Accordingly, amended claim 12 recites that "*Z is independently selected from the group consisting of hydrogen and alkali metal ion*." Applicant further amends claim 12 to specify that the subject is human and to recite that "*the conscious sedated state is produced in the human subject by administering to the human subject at least one parenteral bolus injection in an amount of from about 2 mg/kg to less than 15 mg/kg*". The withdrawn claims have been similarly amended.

New claims 37 and 38 specify that Z is alkali metal ion and the dosages are about 5 mg/kg to about 10 mg/kg, and about 5 mg/kg to about 7.5 mg/kg, respectively. New claim 39 specifies that the compound is O-phosphonooxymethyl propofol disodium salt.

Support for the amendments is found throughout the specification, *inter alia*, at ¶ 31. No new matter is added.

Claim Rejections - 35 USC § 103

As a preliminary matter, Applicant wishes to thank Examiners Sutton and Krass for explaining in detail their position with respect to the showing of unexpected results in the exemplification and related matters. In response, Applicant has amended the claims in order to expedite prosecution, and provides the attached Declaration of Ajit Shah, Ph.D. under 37 CFR §1.132 further demonstrating unexpected results. Applicant also submits the attached Diprivan®

(propofol) product label approved by the U.S. Food and Drug Administration in 2001 demonstrating a teaching away in the prior art.

In response to the statements in the Office Action related to the experimental design in the exemplification, Applicant provides the Shah Declaration, which states that the "target controlled infusion (TCI) technique described in these examples mimics a fast bolus injection, and may be used for the purpose of achieving the same maximal electroencephalogram (EEG) effect ("BIS" scores)." (Shah Dec. ¶ 3). Accordingly, Applicant respectfully requests reconsideration of the exemplification.

In response to the statements in the Office Action related to the unexpected results being commensurate in scope with the claims, in order to expedite prosecution Applicant has amended the claims to recite that Z is independently selected from the group consisting of hydrogen and alkali metal ion. Applicant respectfully submits that an exemplification demonstrating the effect of about 5 mg/kg and about 10 mg/kg is commensurate in scope with claims reciting from about 2 mg/kg to less than 15 mg/kg. Likewise, the administration of an infusion preparation of an alkali salt in the exemplification is commensurate in scope with claims reciting administering a compound in its alkali salt or acid form.

In response to the statements regarding the scope of claim 12 (in the last paragraph of page 3 of the Office Action), Applicant has amended the claims to recite that "*the conscious sedated state is produced in the human subject by administering to the human subject at least one parenteral bolus injection in an amount of from about 2 mg/kg to less than 15 mg/kg*." Accordingly, amended claim 12 does not include "inducing sedation using a combination of a slow bolus injection of 1-2 mg/kg followed by a continuous infusion."

Regarding the proposed modification of Lowrie, Applicant submits the attached product

insert for Diprivan® (propofol) from February 2001.[1] On the very first page of the label, the penultimate paragraph states:

> "Undesirable side effects such as cardiorespiratory depression are likely to occur at higher blood concentrations which result from bolus dosing or rapid increases in infusion rates."

Accordingly, not only does Lowrie fail to describe administering a bolus injection in an amount of from about 2 mg/kg to less than 15 mg/kg, as recited in claim 12, but persons skilled in the art would have been led away from administering bolus injections at the time of the invention, particularly at higher doses, given that side effects such as cardiorespiratory depression were considered likely to occur with bolus dosing of propofol. For at least this reason, persons skilled in the art would not have been led to increase the bolus dosage amount described in Lowrie as the Office Action proposes.

Further evidence of the non-obviousness of the method of claim 12 is provided in the accompanying Declaration of Ajit Shah, Ph.D. In his Declaration, Dr. Shah discusses and provides data demonstrating the significant differences in pharmacokinetic and pharmacodynamic profiles of propofol and O-phosphonooxymethyl propofol (Shah Dec. ¶¶ 5-7). "Because of these differences, methods of administering fospropofol disodium for achieving conscious sedation could not have be[en] predicted from data based on propofol." (Shah Dec. ¶ 4).

For at least the foregoing reasons, Applicant submits that the outstanding rejection has been successfully traversed and respectfully requests withdrawal of this rejection. New claims 37-39 are allowable for at least the same reasons. Upon indication of allowable subject matter, Applicant also request reconsideration and withdrawal of the restriction, at least with respect to

[1] http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.Label_ApprovalHistory#apphist

claims 14-19, which have been similarly amended and are allowable at least for the foregoing reasons.

CONCLUSION

Allowance of the instant application is respectfully requested. The Examiner is invited to telephone the undersigned at the number listed below if doing so would be helpful to resolve any outstanding issues.

Respectfully submitted,

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